DNA methylation effects of the Dutch Hunger Winter.[4,8] These findings, in addition to emerging data emphasising the effect of first-trimester weight gain and changes in adiposity on maternal and offspring obesity-related outcomes,[9,10] suggest that a focus on preconception and periconception should constitute the next frontier for prevention of diabetes over the life course.

Matthew W Gillman
Obesity Prevention Program, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA 02215, USA; and the Department of Nutrition, Harvard TH Chan School of Public Health, Boston, MA, USA
matthew_gillman@hms.harvard.edu

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1 Hales CN, Barker DJ. Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia* 1992; **35:** 595–601.
2 Nielsen JH, Haase TN, Jaksch C, et al. Impact of fetal and neonatal environment on beta cell function and development of diabetes. *Acta Obstet Gynecol Scand* 2014; **93:** 1109–22.
3 Poston L, Taylor PD, Nathanielsz P. Influences of maternal obesity on the health of the offspring: a review of animal models. In: Gillman M, Poston L, eds. Maternal Obesity. Cambridge: Cambridge University Press, 2012: 35–44.
4 Lumey LH, Stein AD, Susser E. Prenatal famine and adult health. *Ann Rev Public Health* 2011; **32:** 237–62.
5 Lumey LH, Khalangot MD, Vaiserman AM. Association between type 2 diabetes and prenatal exposure to the Ukraine famine of 1932–33: a retrospective cohort study. *Lancet Diabetes Endocrinol* 2015; published online Sept 3. http://dx.doi.org/10.1016/S2213-8587(15)00279-X.
6 Vallin J, Mesle F, Adamets S, Pyrozhkov S. A new estimate of Ukrainian population losses during the crises of the 1930s and 1940s. *Popul Stud* 2002; **56:** 249–64.
7 de Rooij SR, Roseboom TJ, Painter RC. Famines in the last 100 years: implications for diabetes. *Curr Diab Rep* 2014; **14:** 536.
8 Tobi EW, Goeman JJ, Monajemi R, et al. DNA methylation signatures link prenatal famine exposure to growth and metabolism. *Nat Commun* 2014; **5:** 5592.
9 Karachaliou M, Georgiou V, Roumeliotaki T, et al. Association of trimester-specific gestational weight gain with fetal growth, offspring obesity, and cardiometabolic traits in early childhood. *Am J Obstet Gynecol* 2015; **212:** 502.e1–14.
10 Walter JR, Perng W, Kleinman KP, Rifas-Shiman SL, Rich-Edwards JW, Oken E. Associations of trimester-specific gestational weight gain with maternal adiposity and systolic blood pressure at 3 and 7 years postpartum. *Am J Obstet Gynecol* 2015; **212:** 499.e1–12.

Hyperglycaemia in pregnancy: still a lot to learn

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Hyperglycaemia in pregnancy is an issue of increasing concern to health-care providers and administrators. The first and most obvious reason is its increasing prevalence, mostly due to the same reasons that are driving the epidemic of obesity and type 2 diabetes almost worldwide. The second reason is related to the findings of the HAPO study [1] of strong, continuous associations between maternal glucose concentrations and increased risk of adverse outcomes in their offspring. The study resulted in the development of a new definition of criteria for diagnosis of gestational diabetes, initially proposed by the International Association of Diabetes and Pregnancy Study Groups,[2] and later endorsed by WHO, with much debate. The third reason is the emerging evidence that the metabolic changes that result in gestational diabetes and type 2 diabetes might be passed onto future generations.[3]

In *The Lancet Diabetes & Endocrinology*, Diane Farrar and colleagues[4] present important data to supplement what is known about gestational diabetes. The researchers studied the association of hyperglycaemia with adverse outcomes in a similar way to the HAPO study, in a large cohort of south Asian and white British women living in the Bradford area in the UK. Women from south Asian countries with large populations such as Pakistan, India, Sri Lanka, and Bangladesh were poorly represented in the HAPO study, and are known to have high prevalence of type 2 diabetes and gestational diabetes. Therefore, the data presented by Farrar and colleagues are important for a large population of women. The findings confirm those of the HAPO study, and also show a continuous and graded association between concentrations of fasting and 2 h post-load glucose (as measured in a maternal oral glucose tolerance test between gestational week 26 and 28) and the newborn's risk of being large for gestational age (LGA), with high adiposity (measured as the sum of skinfolds >90th percentile), and for the women having a caesarean section. The results also show important differences between south Asian and white British women.

Farrar and colleagues report that the glucose concentrations that were associated with increased risk for certain adverse outcomes differed between the south Asian and the British women.[4] For example, the thresholds of fasting plasma glucose that defined a woman's risk of having an infant with birthweight greater than the 90th percentile were 5·6 mmol/L for white British versus 5·1 mmol/L for south Asian women.

The findings could point to differences in the effect that maternal glycaemia has in groups with different genetic or environmental exposures. However, the results might also be due to additional factors related to glucose, such as maternal bodyweight and fat mass, gestational weight gain, and lipid concentrations. Researchers have yet to ascertain the most important factors affecting offspring metabolic health in adulthood.

In Farrar and colleagues' study, the incidence of LGA babies was only about a third in the south Asian group compared with the white British group, whereas babies with sum of skinfolds greater than the 90th percentile did not differ between groups.[4] Similar findings have been published before[5] and could point to important differences between the two ethnic groups. Previous findings have shown that newborns of south Asian women generally have lower birthweight and a higher tendency to be small for gestational age than do newborns of white women. Not only large-for-gestational-age babies but also small-for-gestational-age babies have increased risk for obesity, insulin resistance, and type 2 diabetes in adulthood. Some of the most important early findings showing this phenomenon came from Barker's studies of children born almost 100 years ago.[6] The findings have since been confirmed in different populations, and including in Indian children in the prospective Pune Maternal Nutrition Study.[7] Researchers noted that small and thin Indian babies were more adipose than larger English babies, and they had higher risk of future type 2 diabetes that was associated with insulin resistance at birth. The U-shaped association between birthweight and adult risk of type 2 diabetes has been ascribed to maternal nutritional factors, and recent research has focused on possible links via epigenetic mechanisms whereby environmental exposures in utero might lead to changes in offspring DNA (methylation, histone modifications, and microRNAs).[8]

The first criteria to diagnose gestational diabetes were established to identify pregnant women who were at increased risk for development of type 2 diabetes after pregnancy.[9] Although there is a shift to changing the criteria to focus on infant outcomes, the risk of the mother is still important, as women who have been diagnosed with gestational diabetes are among those with the highest risk of developing type 2 diabetes later in life. In view of findings of intervention studies showing that programmes focusing on healthy nutrition and increased physical activity can reduce the risk for developing type 2 diabetes by about 50% in such high risk groups,[10] health-care providers have to face the challenge to take care of both the women and the children during and after birth.

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Kåre I Birkeland
Department of Endocrinology, Morbid obesity and Preventive Medicine, Oslo University Hospital and Faculty of Medicine, University of Oslo, 0424 Oslo, Norway
k.i.birkeland@medisin.uio.no

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1 Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. New England Journal of Medicine 2008; **358:** 1991–2002.
2 Metzger BE, Gabbe SG, Persson B, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010; **33:** 676–82.
3 Nolan CJ, Damm P, Prentki M. Type 2 diabetes across generations: from pathophysiology to prevention and management. *Lancet* 2011; **378:** 169–81.
4 Farrar D, Fairley L, Santorelli G, et al. Association between hyperglycaemia and adverse perinatal outcomes in south Asian and white British women: analysis of data from the Born in Bradford cohort. *Lancet Diabetes Endocrinol* 2015; published online Sept 7. http://dx.doi.org/10.1016/ S2213-8587(15)00282-X.
5 Sletner L, Nakstad B, Yajnic CS, et al. Ethnic differences in neonatal body composition in a multi-ethnic population and the impact of parental factors: a population-based cohort study. *PLOS One* 2013; **8:** e73058.
6 Hales CN, Barker DJP, Clark PMS, et al. Fetal and infant growth and impaired glucose tolerance at age 64. *BMJ* 1991; **303:** 1019–22.
7 Yajnic CS. Transmission of obesity-adiposity and related disorders from the mother to the baby. *Ann Nutr Metab* 2014; **64** (suppl 1)**:** 8–17.
8 Ling C, Groop L. Epigenetics: a molecular link between environmental factors and type 2 diabetes. *Diabetes* 2009; **58:** 2718–25.
9 O'Sullivan JB, Mahan C. Criteria for oral glucose toleracne test in pregnancy. *Diabetes* 1964; **13:** 278–85.
10 Diabetes Prevention Program Research Group. Reduction in the incidence of type diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002; **346:** 393–403.